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**REMARKS/ARGUMENTS**

Claims 1-8 and 10-33 are pending in the application.

Claims 2, 5-8, 9, 10-17 have been canceled without prejudice or waiver .

Claims 1, 3, 4, 18, 19 and 21-33 stand rejected.

In view that this application has been granted CIP status from US serial No. 09/017,412 now US Patent No. 6,270,964 (see below), it is respectfully submitted that there is sufficient guidance in the earlier application as to the selection of a reporter molecule as well as sufficient Examples of the types of reporters that are desirable. Furthermore, the patent statute is also clear regarding enablement. As long as there is sufficient guidance from the specification, there is really no requirement for an example, however Applicant has provided Examples to illustrate the invention.

Applicant also has shown in its prior US patent No. 6,270,964; how to select, enable and design a reporter molecule and what are the requirements for successfully performing a PCA using the multitude of reporters which have been exemplified. For the Examiners' benefit those design requirements are outlined below (See from col. 3 , line 58 to col. 4, line 42:

"One particular strategy for designing a protein complementation assay (PCA) is based on using the following characteristics: 1) A protein or enzyme that is relatively small and monomeric, 2) for which there is a large literature of structural and functional information, 3) for which simple assays exist for the reconstitution of the protein or activity

of the enzyme, both in vivo and in vitro, and 4) for which overexpression in eukaryotic and prokaryotic cells has been demonstrated. If these criteria are met, the structure of the enzyme is used to decide the best position in the polypeptide chain to split the gene in two, based on the following criteria: 1) The fragments should result in subdomains of continuous polypeptide; that is, the resulting fragments will not disrupt the subdomain structure of the protein, 2) the catalytic and cofactor binding sites should all be contained in one fragment, and 3) resulting new N- and C-termini should be on the same face of the protein to avoid the need for long peptide linkers and allow for studies of orientation-dependence of protein binding.

It should be understood that the above mentioned criteria do not all need to be satisfied for a proper working of the present invention. It is an advantage that the enzyme be small, preferably between 10-40 kDa. Although monomeric enzymes are preferred, multimeric enzymes can also be envisaged as within the scope of the present invention.

The dimeric protein tyrosinase can be used in the instant assay. The information on the structure of the enzyme provides an additional advantage in designing the PCA, but is not necessary. Indeed, an additional strategy, to develop PCAs is presented, based on a combination of exonuclease digestion-generated protein fragments followed by directed protein evolution in application to the enzyme aminoglycoside kinase. Although the overexpression in prokaryotic cells is preferred it is not a necessity. It will be understood to the skilled artisan that the enzyme catalytic site (of the chosen enzyme)

does not absolutely need to be on same molecule.

The '964 patent explains the rationale and criteria for using a particular enzyme in a PCA. FIG. 1 shows a general description of a PCA. The gene for a protein or enzyme is rationally dissected into two or more fragments. Using molecular biology techniques, the chosen fragments are subcloned, and to the 5' ends of each, proteins that either are known or thought to interact are fused. Co-transfection or transformation these DNA constructs into cells is then carried out. Reassembly of the probe protein or enzyme from its fragments is catalyzed by the binding of the test proteins to each other, and reconstitution is observed with some assay. It is crucial to understand that these assays will only work if the fused, interacting proteins catalyze the reassembly of the enzyme. That is, observation of reconstituted enzyme activity must be a measure of the interaction of the fused proteins."

#### **PRIORITY**

Regarding priority, The Examiners' attention is called to the interview summary of January 6, 2004 granting CIP status.

#### **THE REJECTION UNDER 35 U.S.C. § 102(b), 35 U.S.C. § 102(e) AND 103(a)**

It is believed that by granting the CIP status, that all the above rejections are now moot.

### **DOUBLE PATENTING**

The Examiner further expresses concerns over possible double patenting issues arising from the '964 claims. The claims of the '964 patent are directed to methods for detecting protein-protein interactions. Hence the claims of the present application will not have any double patenting problems given that they are methods to identify sets of molecules capable of such interactions and include steps for that identification of such sets of molecules in a single panel-panel screening.

Regarding the draftsman requirement for corrections, Applicant will submit formal drawings after allowable subject matter is indicated.

Also regarding a new oath or declaration, Applicant will submit a new oath after allowable subject matter is indicated. In any event due to the fact that some of the inventors live overseas, representative is in the process of preparing the new declarations and submitting it to the inventors.

In view of the above remarks, it is respectfully submitted that the claims are now in condition for allowance. Reconsideration and withdrawal of the rejections and objections are requested. The Examiner is invited to contact the undersigned at 703-418-2777 if he feels that further discussion may facilitate the resolution of any outstanding issues.

An early indication of a Notice of Allowance is earnestly solicited.

Respectfully submitted,

  
A handwritten signature in black ink, appearing to read "Isaac Angres", is written over a horizontal line.

Isaac Angres  
Reg. No. 29,765

Date: January 21, 2004  
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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
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EXAMINER
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ART UNIT	PAPER NUMBER
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DATE MAILED:

INTERVIEW SUMMARY

All participants (applicant, applicant's representative, PTO personnel):

- (1) Isaac Angres (3) \_\_\_\_\_  
(2) Andrew Wang (4) \_\_\_\_\_

Date of Interview 1/6/04

Type: ☐ Telephonic ☒ Personal (copy is given to ☐ applicant ☒ applicant's representative).

Exhibit shown or demonstration conducted: ☐ Yes ☒ No If yes, brief description: \_\_\_\_\_

Agreement ☒ was reached. ☐ was not reached.

Claim(s) discussed: all

Identification of prior art discussed: Pelletier

Description of the general nature of what was agreed to if an agreement was reached, or any other comments: It was agreed that ~~priority~~ CIP status should be granted. ~~Agreed~~ to since appl was filed prior to 11/29/2000. I will discuss w/ ex. prior art and let them it should apply w/ the CIP status

(A fuller description, if necessary, and a copy of the amendments, if available, which the examiner agreed would render the claims allowable must be attached. Also, where no copy of the amendments which would render the claims allowable is available, a summary thereof must be attached.)

1. ☐ It is not necessary for applicant to provide a separate record of the substance of the interview.

Unless the paragraph above has been checked to indicate to the contrary. A FORMAL WRITTEN RESPONSE TO THE LAST OFFICE ACTION IS NOT WAIVED AND MUST INCLUDE THE SUBSTANCE OF THE INTERVIEW. (See MPEP Section 713.04). If a response to the last Office action has been ready been filed, APPLICANT IS GIVEN ONE MONTH FROM THIS INTERVIEW DATE TO FILE A STATEMENT OF THE SUBSTANCE OF THE INTERVIEW.

2. ☐ Since the Examiner's interview summary above (including any attachments) reflects a complete response to each of the objections, rejections and requirements that may be present in the last Office action, and since the claims are now allowable, this completed form is considered to fulfill the response requirements of the last Office action. Applicant is not relieved from providing a separate record of the interview unless box 1 above is also checked.

Examiner Note: You must sign this form unless it is an attachment to another form.